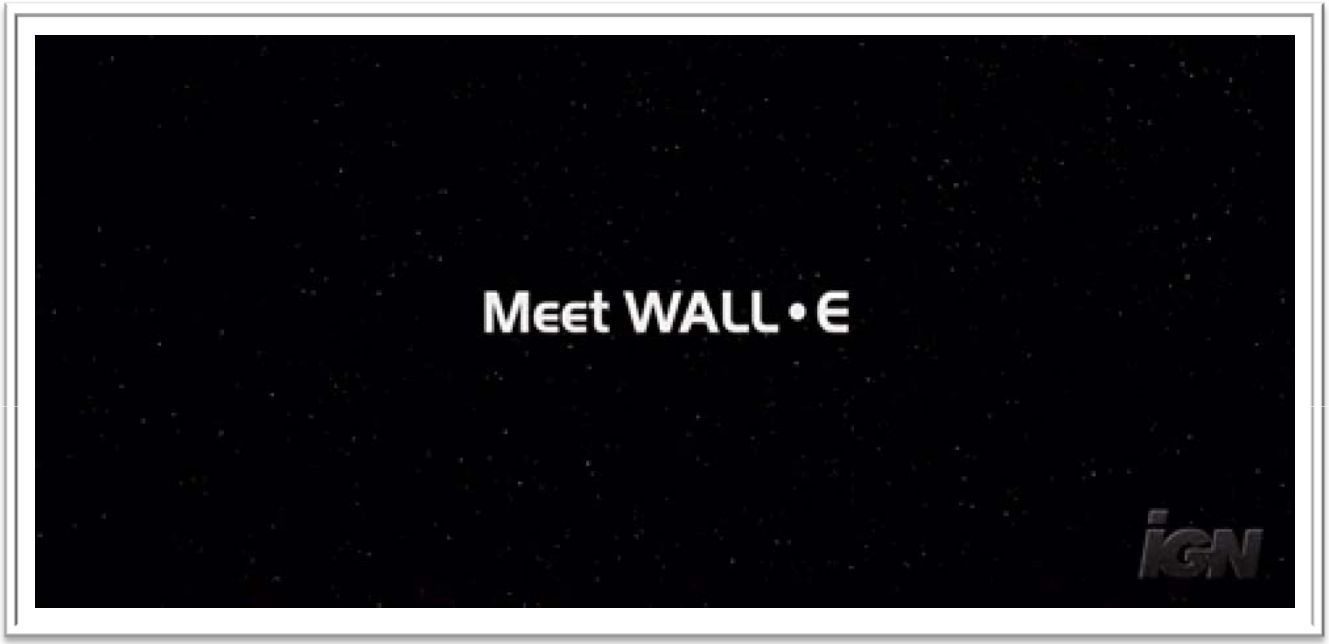
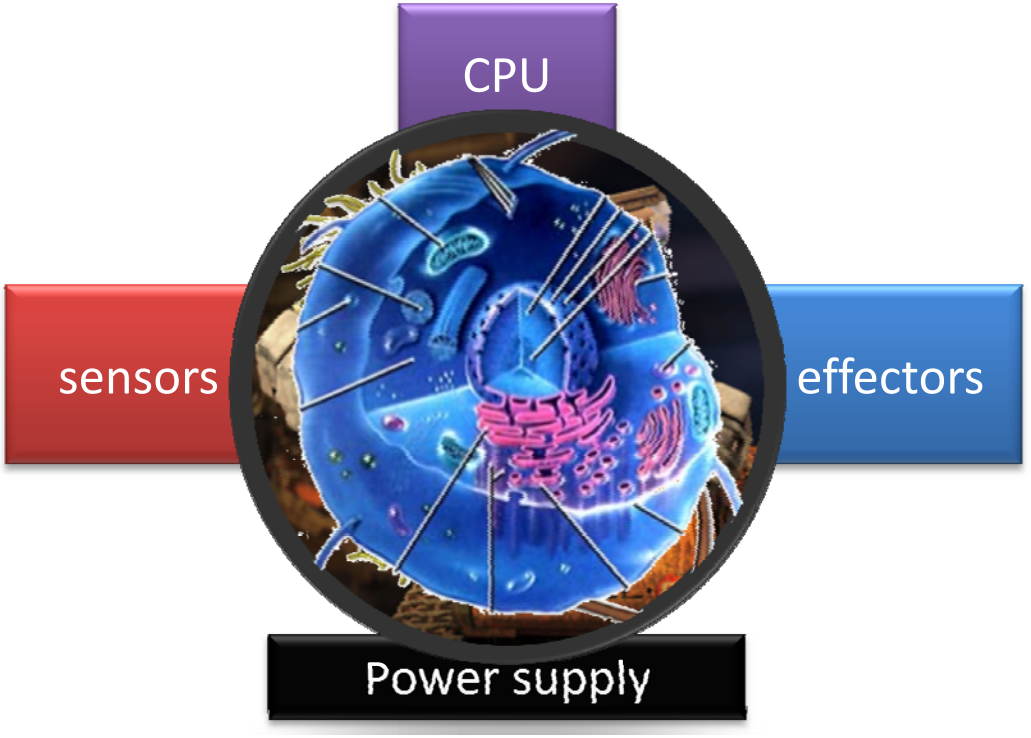
Natalie Kuldell and Ron Weiss

February 2nd, 2010

http://openwetware.org/wiki/20.20(S10)

Biological Engineering Analogy: bioRobotics





2020: Futurists

Freeman Dyson writes:

"Biotechnology will become as domesticated as computer games and children and housewives will create their new animal and plant species at home."

Quack? Genius?

2020: Futurists

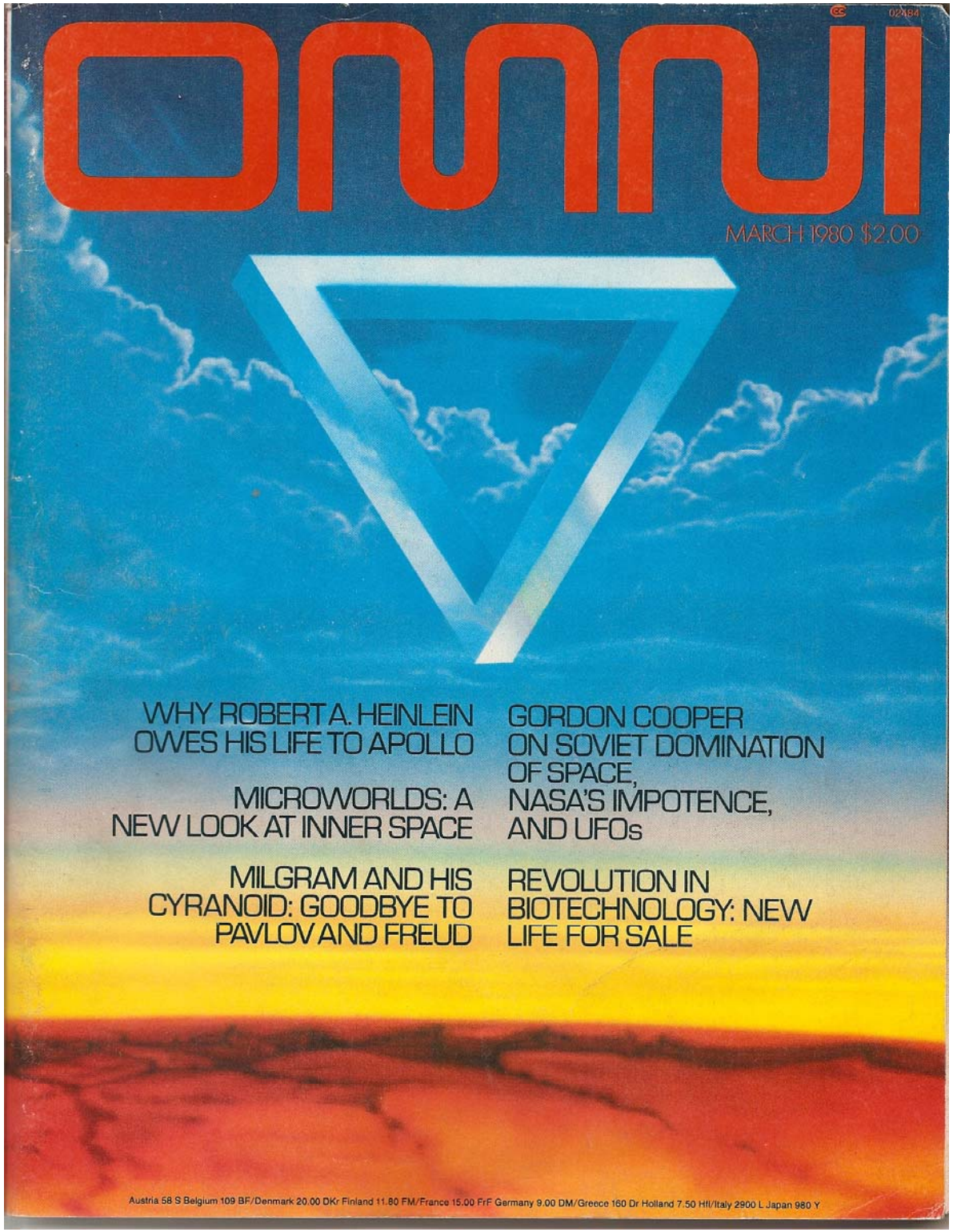
Freeman Dyson writes:

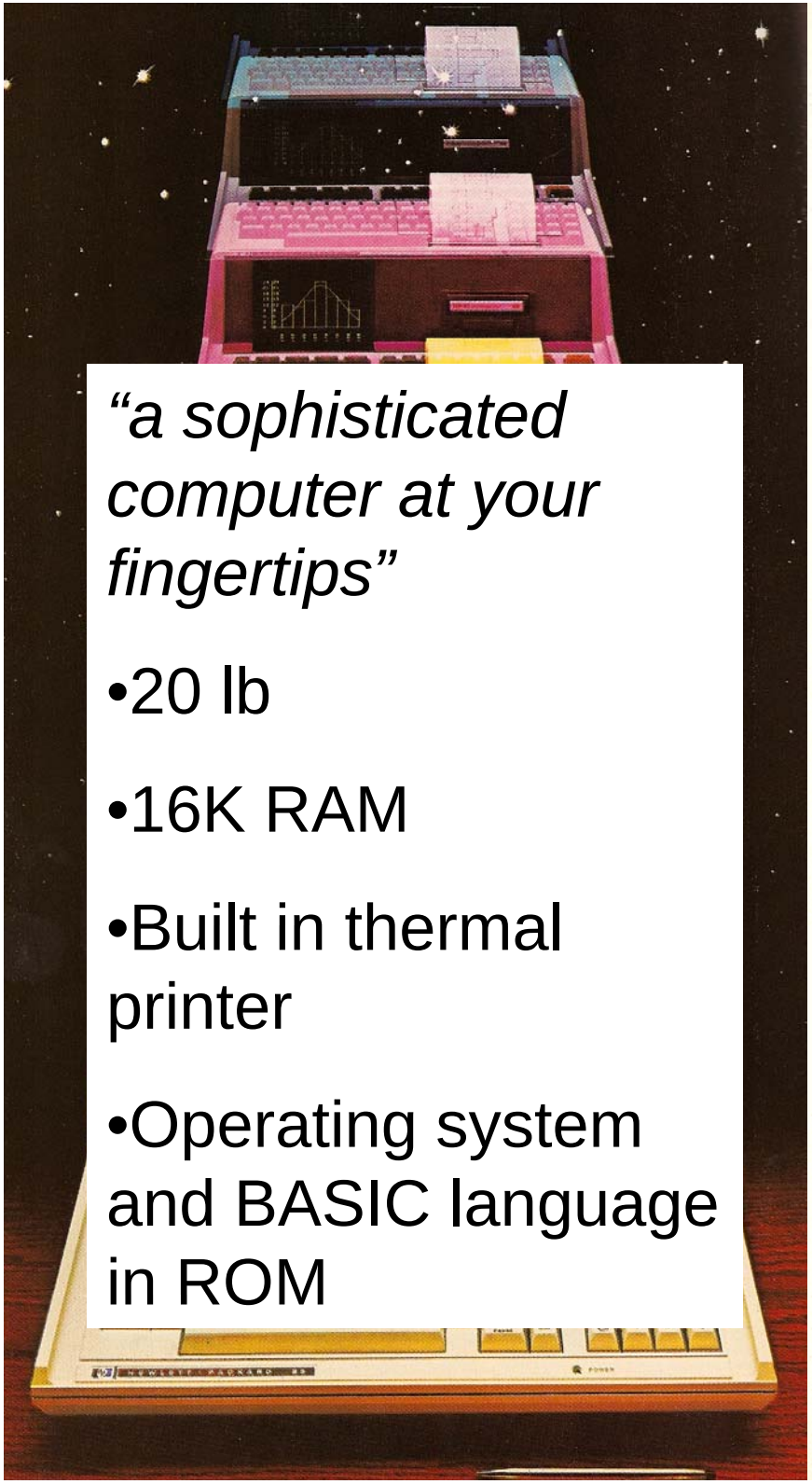
"Biotechnology will become as domesticated as computer games and children and housewives will create their new animal and plant species at home.

Quack? Genius?

MIT Human Ecology Design team

2020: Historians





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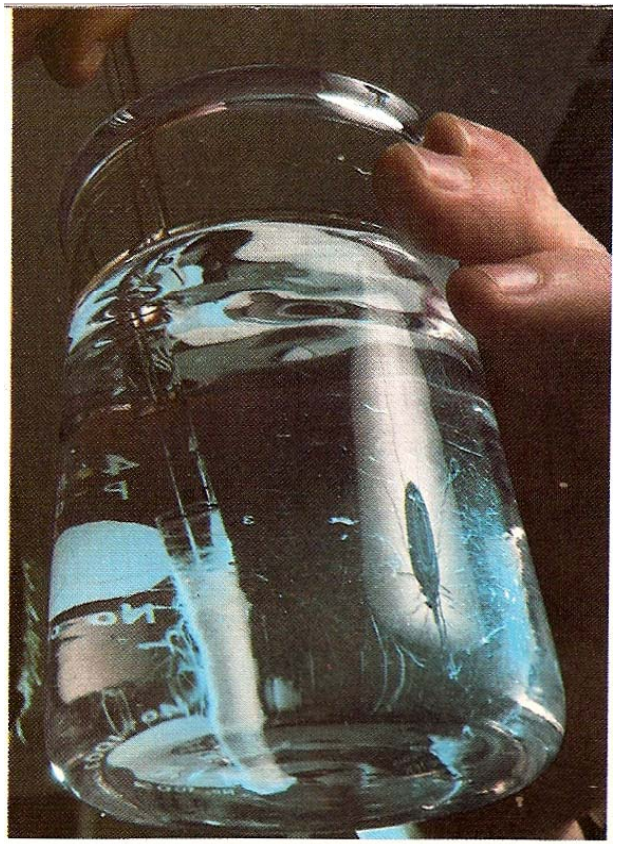
“a scientist clad in white spools threads of DNA onto a glass rod. He is about to treat it with enzymes, then insert it into E. coli, endowing the microbe with powers nature never gave it.”



From a chilled beaker, a scientist clad in white gently spools spaghettilike threads of DNA onto a glass rod. He is about to treat it with enzymes that will clip away all but a chosen gene, then insert it into the genetic material of a bacterium called *Escherichia coli*, endowing the microbe with powers that nature never gave it.

Not long ago experiments with recombinant DNA stirred visions of strange, artificial diseases against which humanity would have no natural defense; such experiments provoked sharp controversy over whether scientists should be allowed to tamper with life itself. Today most of the fears have died down, and biotechnology is filling the heads of businessmen with visions of immense profits.

In the past ten years or so, dozens of new companies have begun to harness the life processes and put them to work in industry. Quietly, almost unnoticed in a world dazzled by innovative electronic products, these firms are fomenting a technological revolution that promises to shake the foundations of medicine, agriculture, food processing, energy production, and the chemical and pharmaceutical industries.

Already included among biotechnology's success stories are bacteria engineered to produce human insulin, drug-delivery systems that

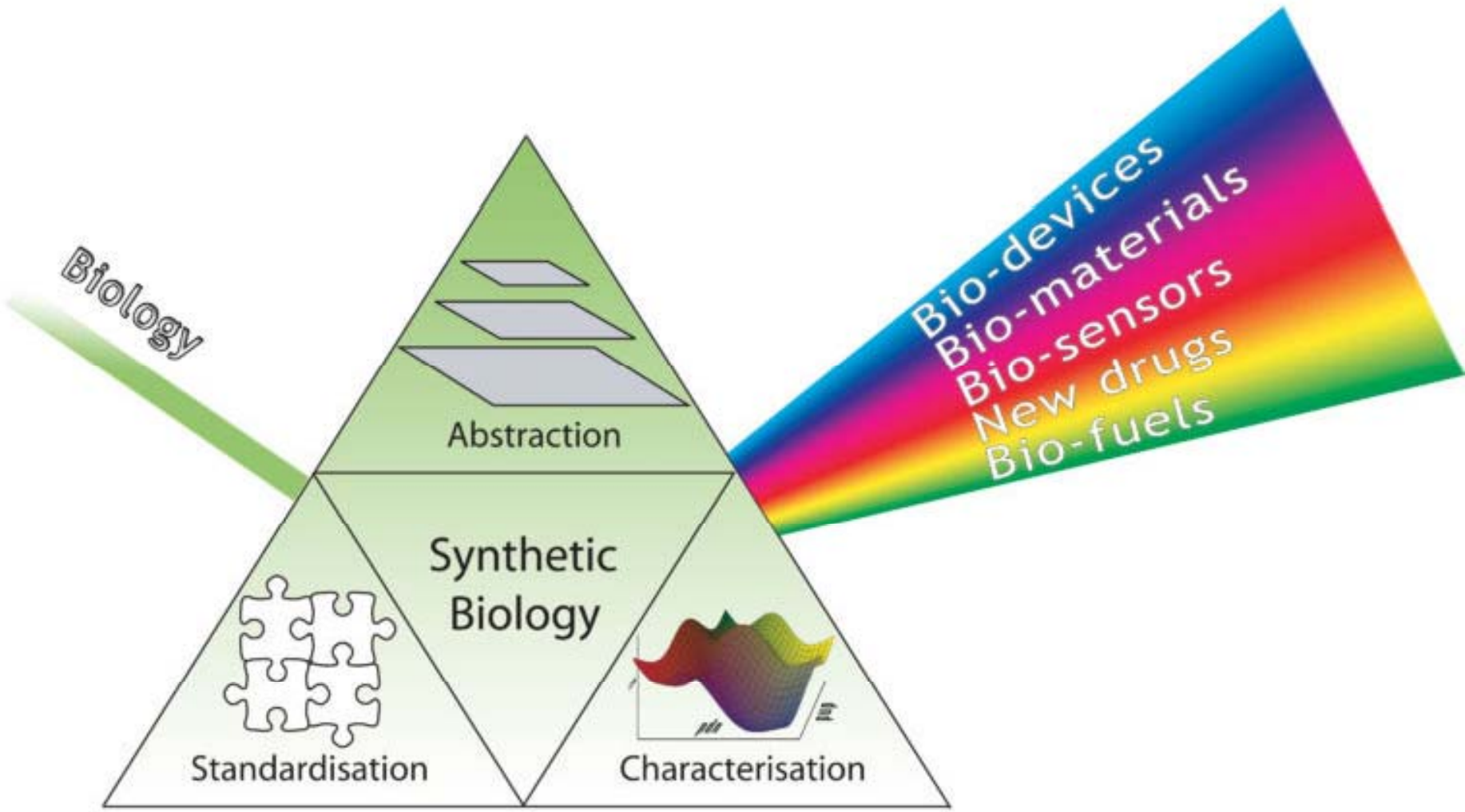
THE GENE TRUST

BY KATHLEEN AND SHARON McAULIFFE

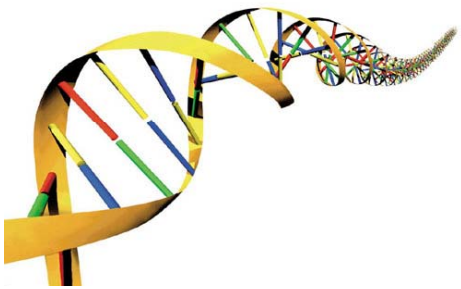
Science and business join forces to exploit the machinery of life

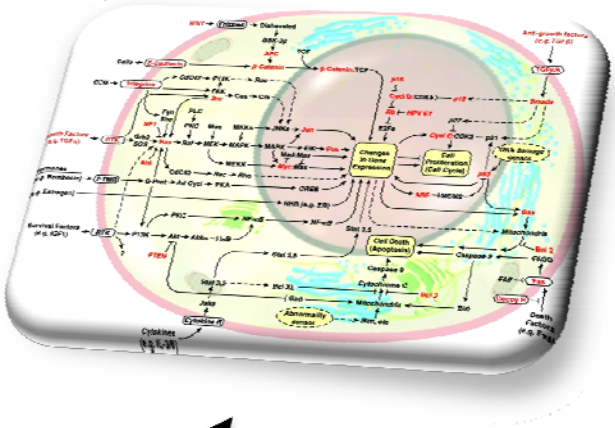
PHOTOGRAPHS BY DOUGLAS KIRKLAND

What's new: Application of engineering principles to biology



From idea to implementation





Postcards & snapshots so far

- DNA based memory

Construction of a genetic toggle switch in *Escherichia coli*

Timothy S. Gardner*†, Charles R. Cantor* & James J. Collins*†

** Department of Biomedical Engineering, † Center for BioDynamics and ‡ Center for Advanced Biotechnology, Boston University, 44 Cummington Street, Boston, Massachusetts 02215, USA*

NATURE | VOL 403 | 20 JANUARY 2000 | www.nature.com

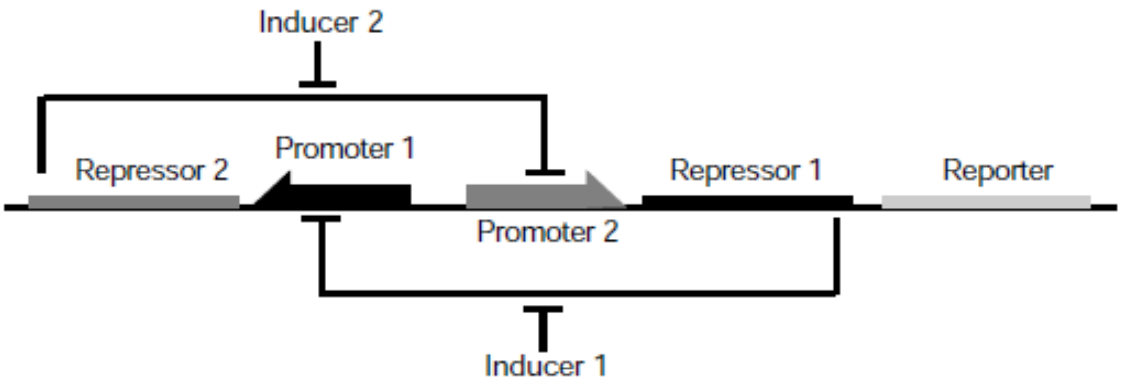
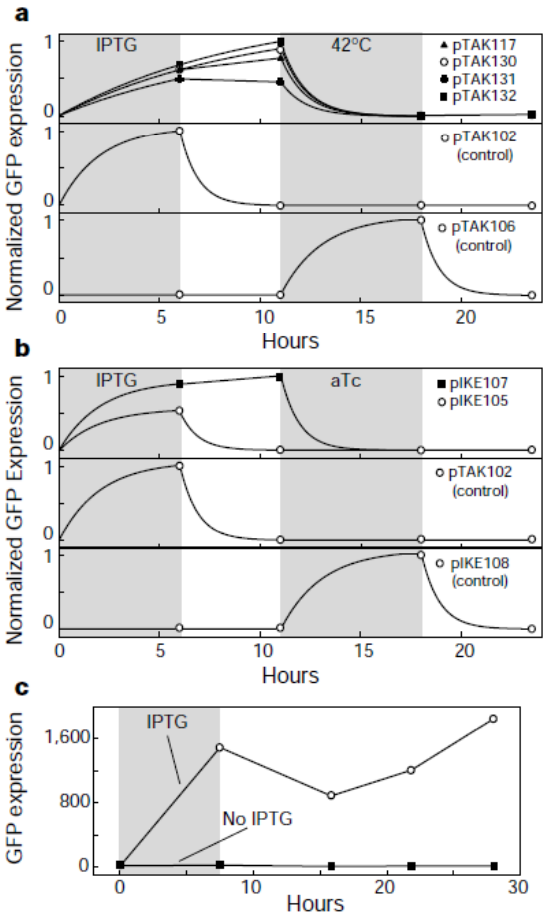


Figure 1 Toggle switch design. Repressor 1 inhibits transcription from Promoter 1 and is induced by Inducer 1. Repressor 2 inhibits transcription from Promoter 2 and is induced by Inducer 2.



Postcards & snapshots so far

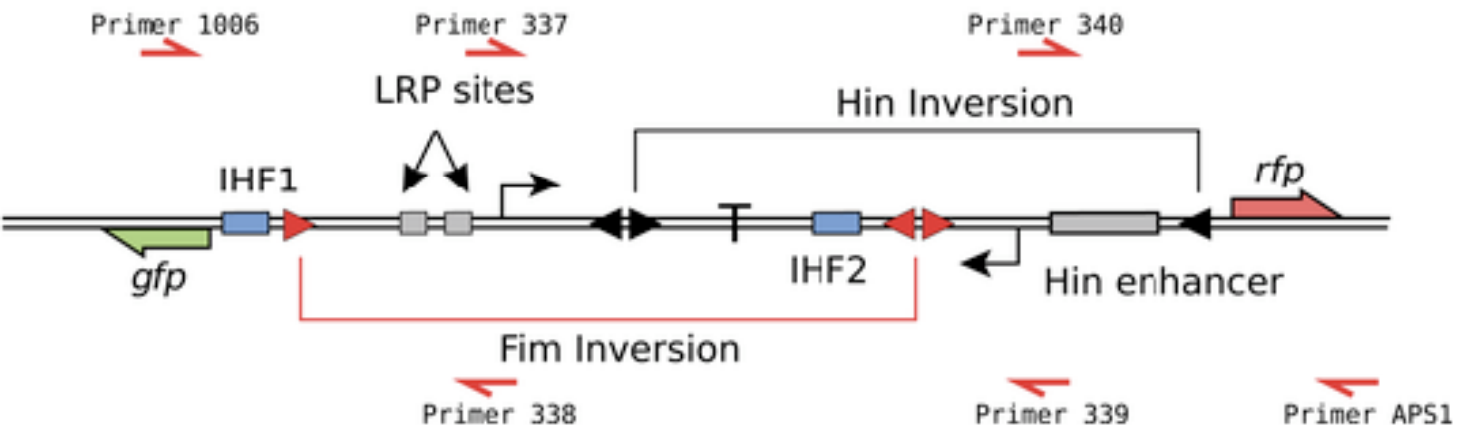
- DNA based memory

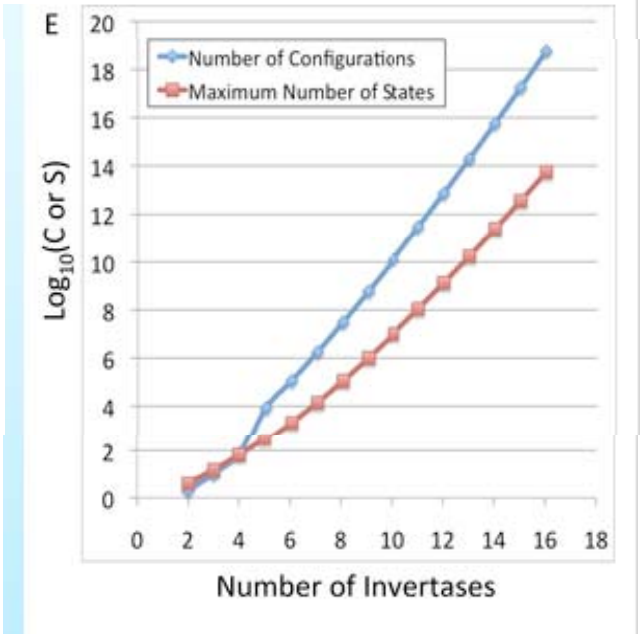
RESEARCH ARTICLE

Design and Construction of a Double Inversion Recombination Switch for Heritable Sequential Genetic Memory

Timothy S. Ham[1], Sung K. Lee[2], Jay D. Keasling[1,2,3], Adam P. Arkin[1,2*]

Citation: Ham TS, Lee SK, Keasling JD, Arkin AP (2008) Design and Construction of a Double Inversion Recombination Switch for Heritable Sequential Genetic Memory. PLoS ONE 3(7): e2815. doi:10.1371/journal.pone.0002815





Postcards & snapshots so far

- DNA based memory
- circuit engineering

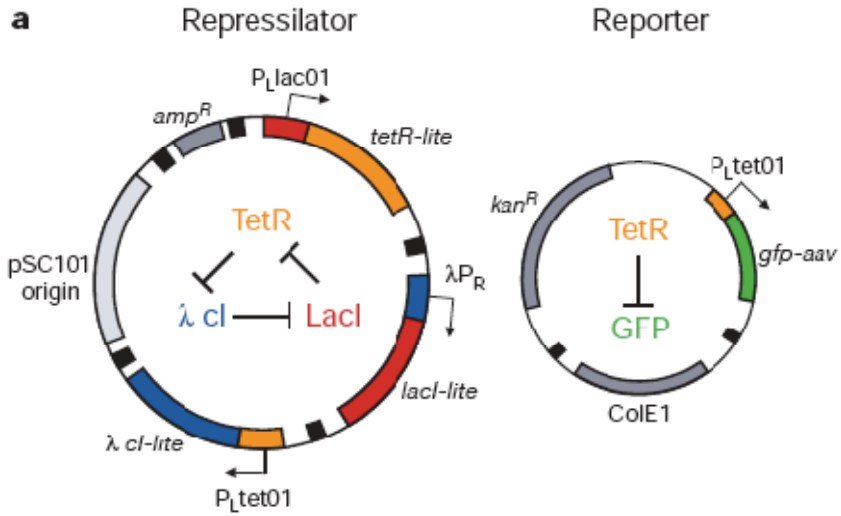
A synthetic oscillatory network of transcriptional regulators

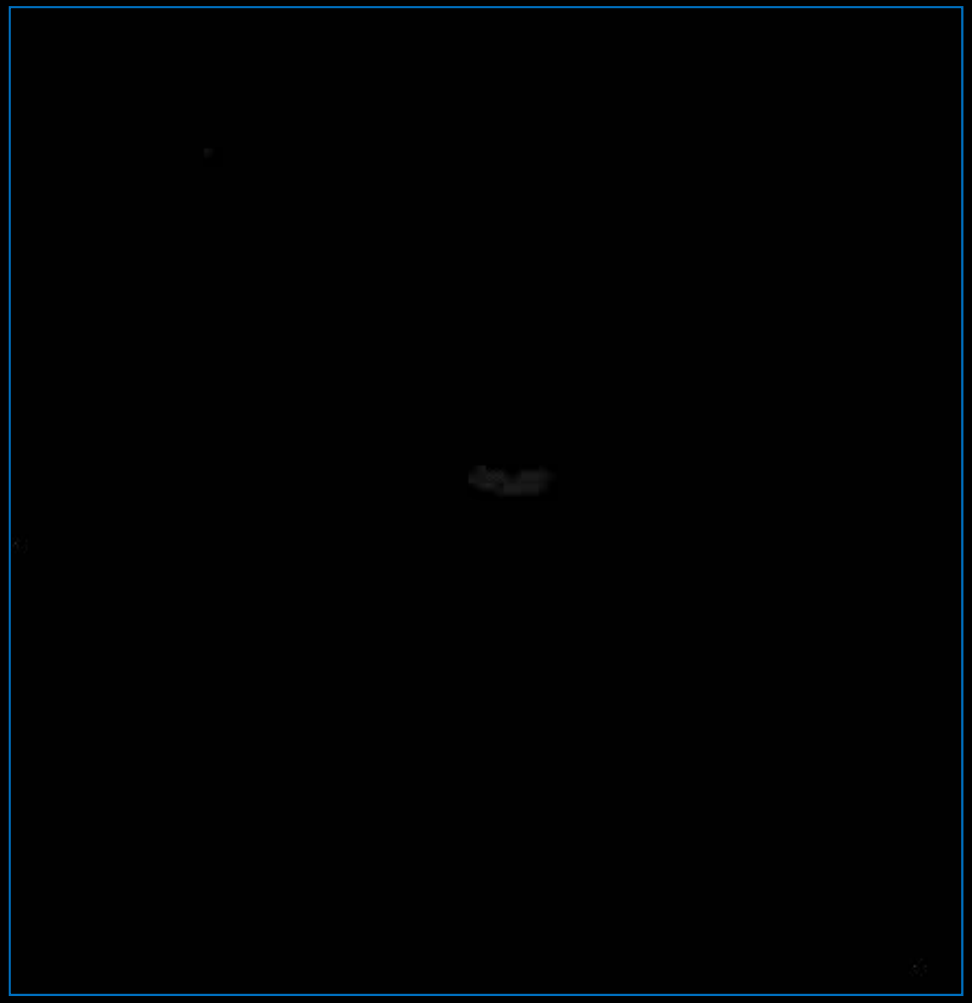
Michael B. Elowitz & Stanislas Leibler

Departments of Molecular Biology and Physics, Princeton University, Princeton, New Jersey 08544, USA

Networks of interacting biomolecules carry out many essential functions in living cells[1], but the 'design principles' underlying the functioning of such intracellular networks remain poorly understood, despite intensive efforts including quantitative analysis of relatively simple systems[2]. Here we present a complementary approach to this problem: the design and construction of a synthetic network to implement a particular function. We used three transcriptional repressor systems that are not part of any natural biological clock[3–5] to buil

NATURE | VOL 403 | 20 JANUARY 2000 | www





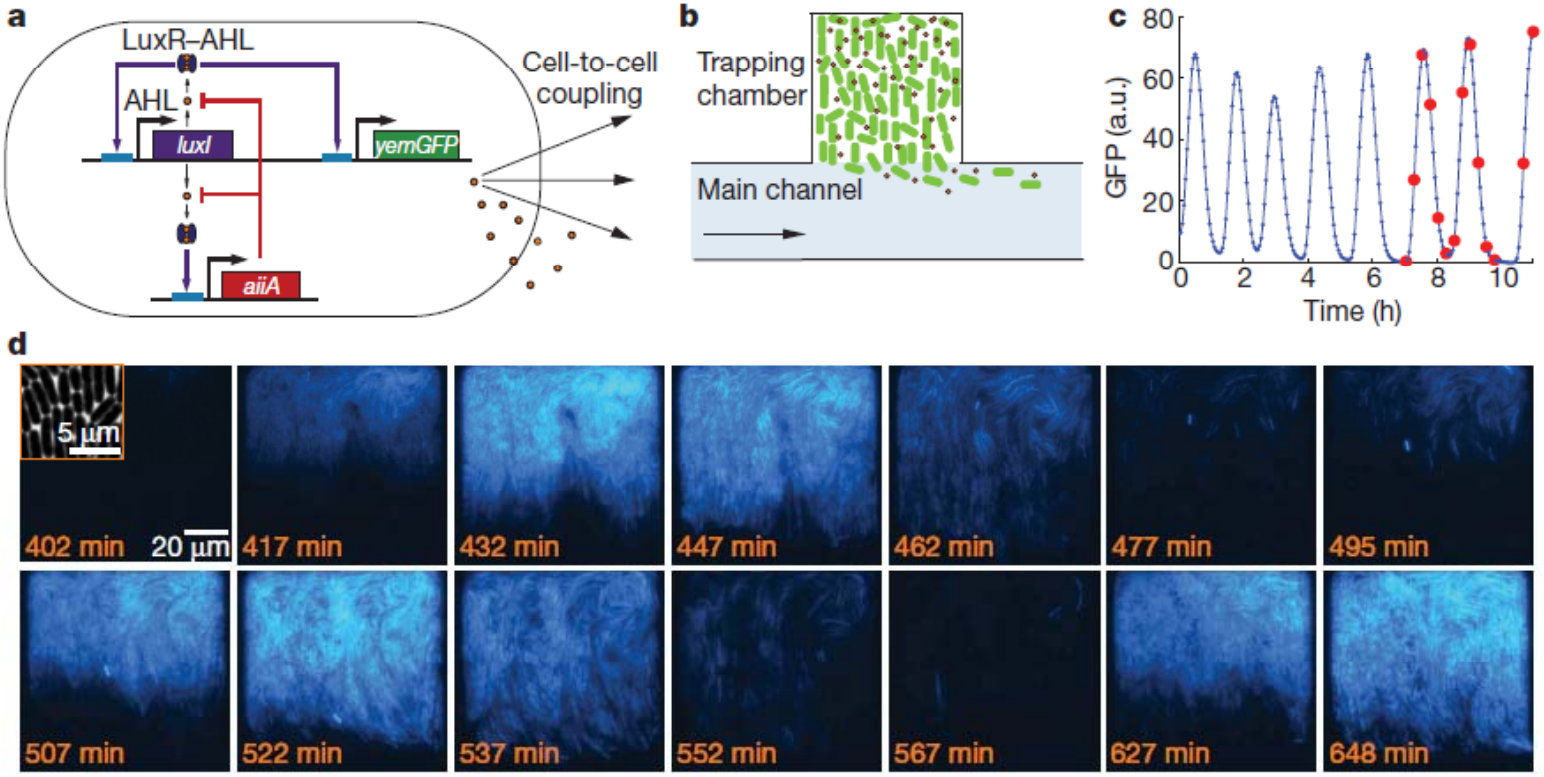
Postcards & snapshots so far

A synchronized quorum of genetic clocks

Tal Danino[1]*, Octavio Mondragón-Palomino[1]*, Lev Tsimring[2] & Jeff Hasty[1,2,3]

- DNA based memory
- circuit engineering

NATURE | Vol 463 | 21 January 2010

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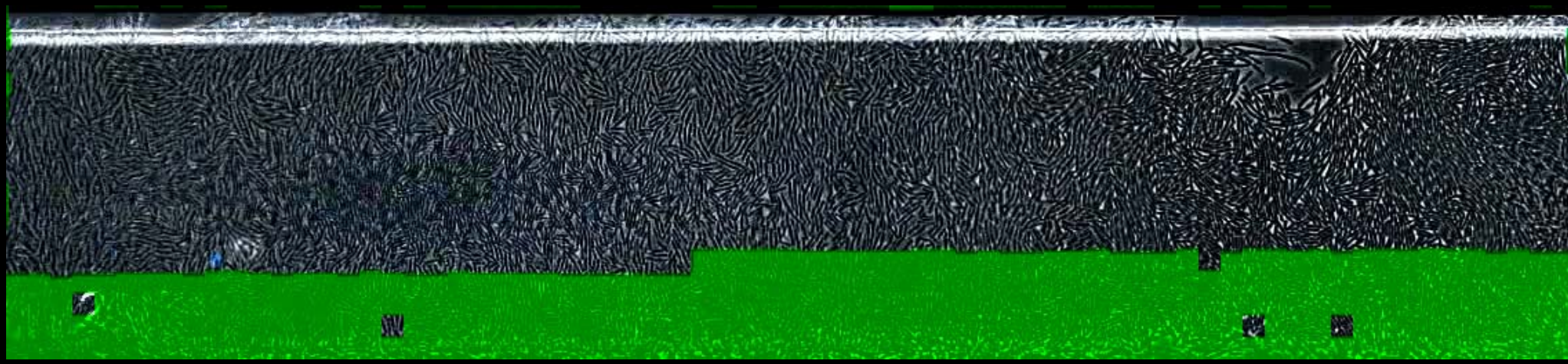


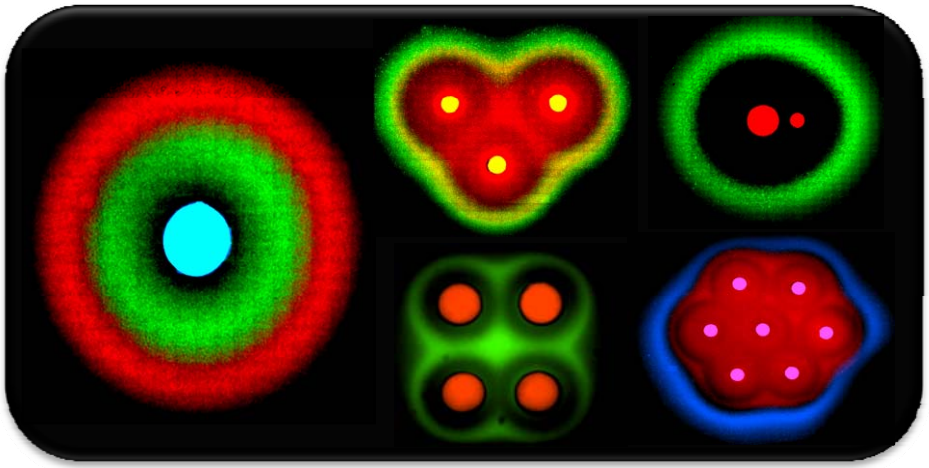
Postcards & snapshots so far

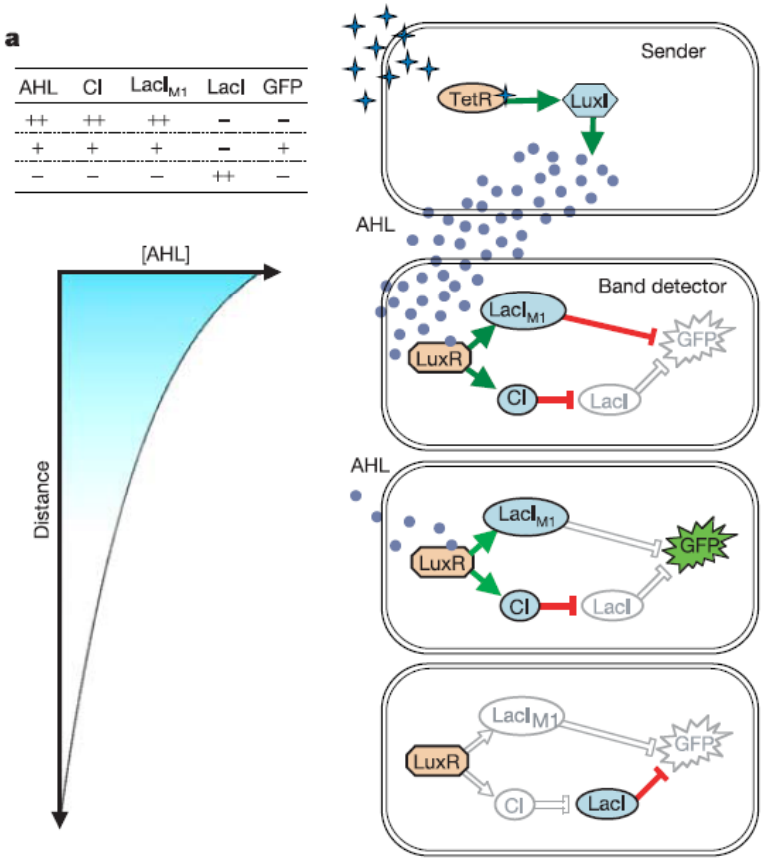
- DNA based memory
- circuit engineering

A synthetic multicellular system for programmed pattern formation

Subhayu Basu[1], Yoram Gerchman[1], Cynthia H. Collins[3], Frances H. Arnold[3] & Ron Weiss[1,2]

NATURE | VOL 434 | 28 APRIL 2005 | www.nature.com/nature





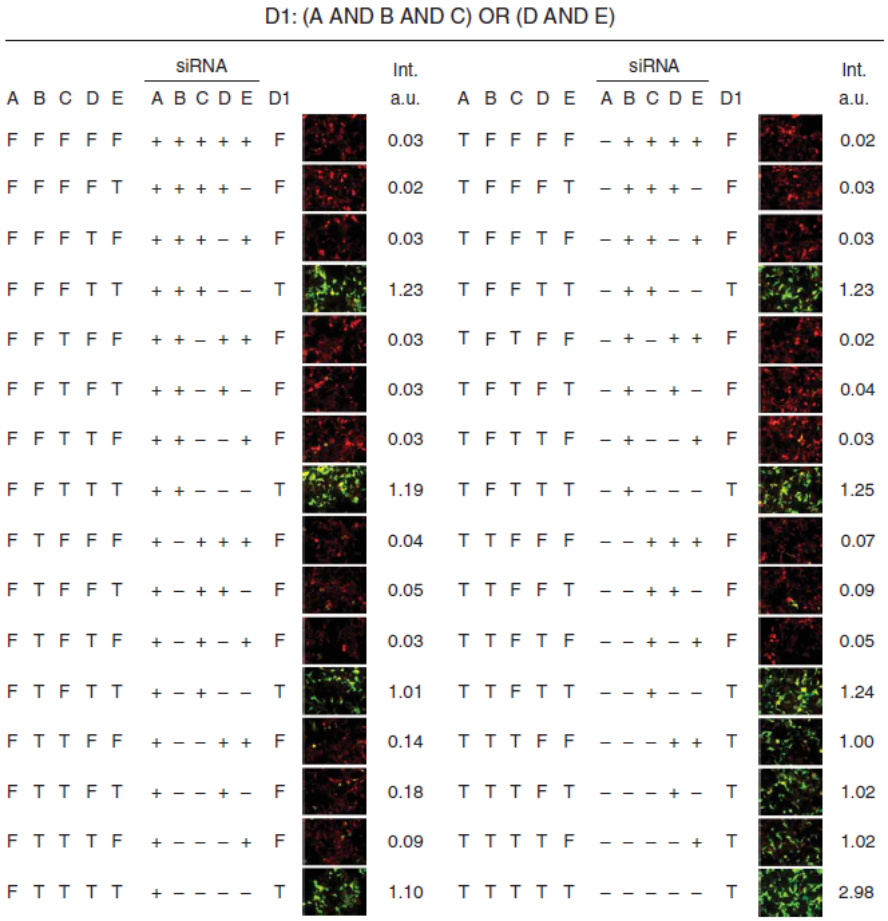
Postcards & snapshots so far

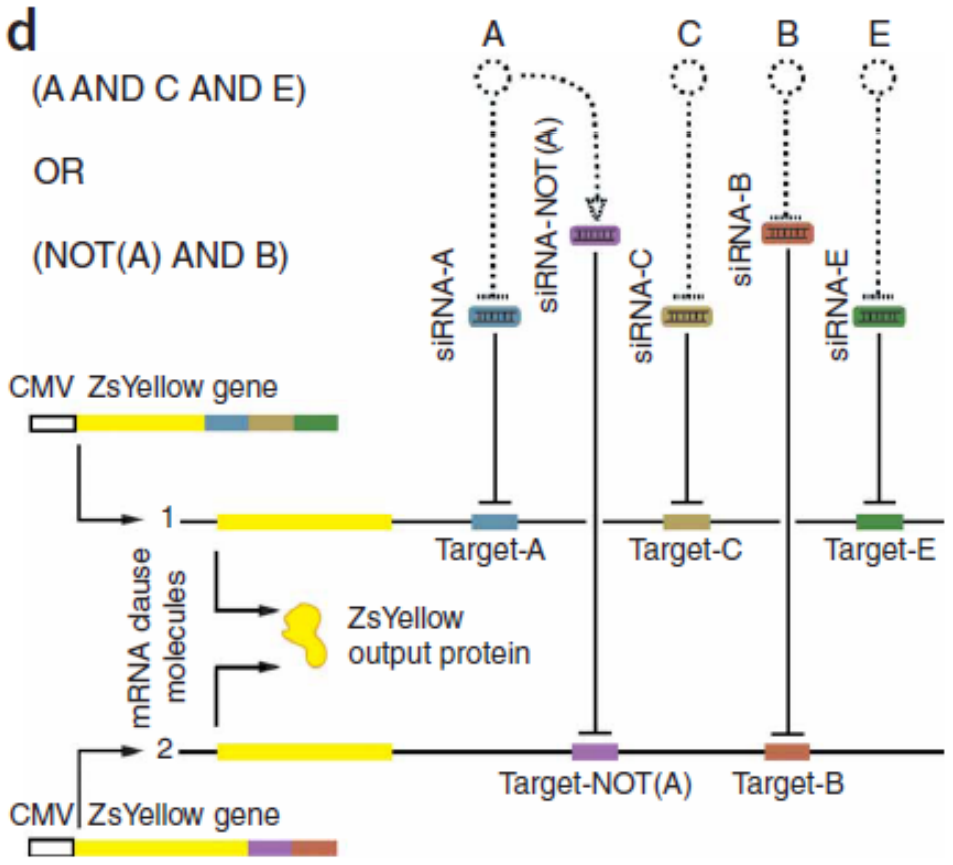
- logic engineering

A universal RNAi-based logic evaluator that operates in mammalian cells

Keller Rinaudo[1,4], Leonidas Bleris[1,4], Rohan Maddamsetti[1], Sairam Subramanian[2,3], Ron Weiss[2,3] & Yaakov Benenson[1]

NATURE BIOTECHNOLOGY VOLUME 25 NUMBER 7 JULY 2007





Postcards & snapshots so far

- DNA based memory
- circuit engineering
- logic engineering
- genome re-engineering

Molecular Systems Biology (2005) doi:10.1038/msb4100025

www.molecularsystemsbiology.com

molecular systems biology

Refactoring bacteriophage T7

Leon Y Chan[1,3], Sriram Kosuri[2,3] and Drew Endy[2,*]

A Wild-type T7 *2.8–3* elements

----------*2.8*---------->
acgcaaagggaggcgacatggcaggttacggcgctaaaggaatccgaaa
<--*3*-RBS--><----------*3*----------

B T7.1 parts 28 and 29

acgcaaGgggagAcgacaCggcaggttacggcgctaaggatccggccgcaaacgggaggcgacatggcaggttacggcgctaaa
----------*2.8*----------><D28R|D29L><--3RBS------><----------*3*----

Postcards & snapshots so far

- DNA based memory
- circuit engineering
- logic engineering
- genome re-engineering

Complete Chemical Synthesis, Assembly, and Cloning of a *Mycoplasma genitalium* Genome

Daniel G. Gibson, Gwynedd A. Benders, Cynthia Andrews-Pfannkoch, Evgeniya A. Denisova, Holly Baden-Tillson, Jayshree Zaveri, Timothy B. Stockwell, Anushka Brownley, David W. Thomas, Mikkel A. Algire, Chuck Merryman, Lei Young, Vladimir N. Noskov, John I. Glass, J. Craig Venter, Clyde A. Hutchison III, Hamilton O. Smith*

We have synthesized a 582,970–base pair *Mycoplasma genitalium* genome. This synthetic genome, named *M. genitalium* JCVI-1.0, contains all the genes of wild-type *M. genitalium* G37 except MG408, which was disrupted by an antibiotic marker to block pathogenicity and to allow for selection. To identify the genome as synthetic, we inserted "watermarks" at intergenic sites known

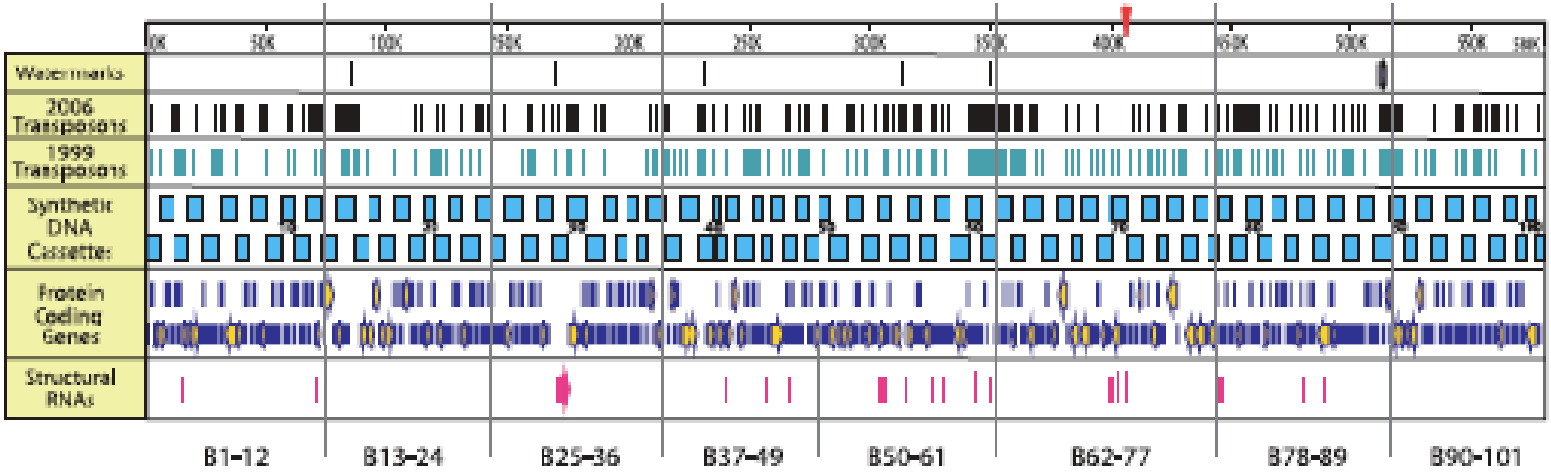


Fig. 1. Linear GenomBench (Invitrogen) representation of the circular 582,970-bp *M. genitalium* JCVI-1.0 genome. Features shown include locations of watermarks and the aminoglycoside resistance marker, visible Tn*4001* transposon insertions determined in our 1999 and 2006 studies (3, 4), overlapping synthetic DNA cassettes that comprise the whole genome sequence, 485 *M. genitalium* protein-coding genes, 43 *M. genitalium* rRNA, tRNA, and structural RNA genes, and B-series assemblies (Fig. 2). The red dagger on the genome coordinates line shows the location of the yeast/*E. coli* shuttle vector insertion. Table S1 lists cassette coordinates; table S2 has FASTA files for all 101 cassettes; table S3 lists watermark coordinates; table S4 lists the sequences of the watermarks.

Postcards & snapshots so far

- DNA based memory
- circuit engineering
- logic engineering
- genome re-engineering

Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus

Terrence M. Tumpey,[1*] Christopher F. Basler,[2] Patricia V. Aguilar,[2] Hui Zeng,[1] Alicia Solórzano,[2] David E. Swayne,[4] Nancy J. Cox,[1] Jacqueline M. Katz,[1] Jeffery K. Taubenberger,[3] Peter Palese,[2] Adolfo García-Sastre[2]

The pandemic influenza virus of 1918–1919 killed an estimated 20 to 50 million people worldwide. With the recent availability of the complete 1918 influenza virus coding sequence, we used reverse genetics to generate an influenza virus bearing all eight gene segments of the pandemic virus to study the properties associated with its extraordinary virulence. In stark contrast to contemporary human influenza H1N1 viruses, the 1918 pandemic virus had the ability to replicate in the absence of trypsin, caused death in mice and embryonated chicken eggs, and displayed a high-growth phenotype in human bronchial epithelial cells. Moreover, the coordinated expression of the 1918 virus genes most certainly confers the unique high-virulence phenotype observed with this pandemic virus.

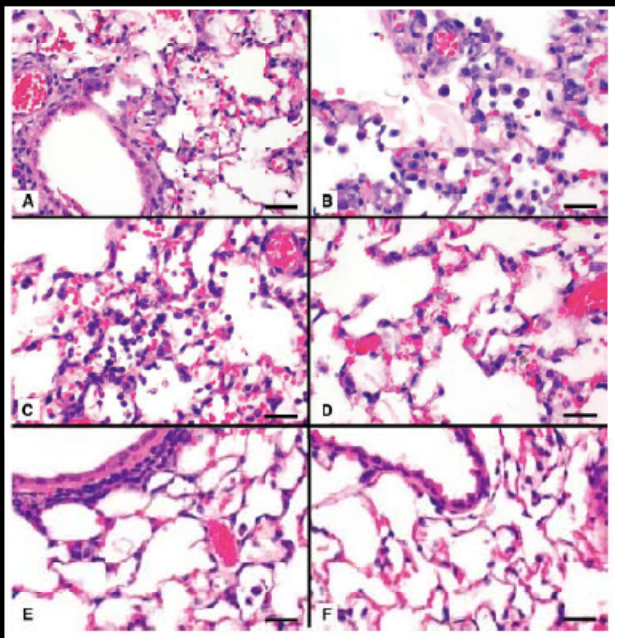


Fig. 2. Photomicrographs of hematoxylin and eosin–stained lung sections. (A to C), lungs from mice infected with the 1918 influenza virus: (A) necrotizing bronchiolitis and severe alveolitis. (B) severe alveolar edema and histiocytic alveolitis with scattered neutrophils, and (C) alveolitis, predominantly neutrophilic, and associated hemorrhage. (D) Moderate alveolitis and edema in lungs from a mouse infected with 1918 HA/NA/M/NP/NS:Tx/91 virus. (E) Mild peribronchial inflammation with adjacent minimal alveolitis in a mouse infected with Tx/91 HA:1918 virus. (F) Lung tissue from a Tx/91–infected mouse showing the paucity of lesions. Scale bars, 25 μm (A) and 15 μm (B to F).

Postcards & snapshots so far

- genome re-engineering
- DNA based memory
- logic engineering
- circuit engineering
- system engineering

Vol 438|24 November 2005 nature

BRIEF COMMUNICATIONS

Engineering *Escherichia coli* to see light

These smart bacteria 'photograph' a light pattern as a high-definition chemical image.

Anselm Levskaya*, Aaron A. Chevalier†, Jeffrey J. Tabor†, Zachary Booth Simpson†, Laura A. Lavery†, Matthew Levy†, Eric A. Davidson†, Alexander Scouras†, Andrew D. Ellington†‡, Edward M. Marcotte†‡, Christopher A. Voigt*§||

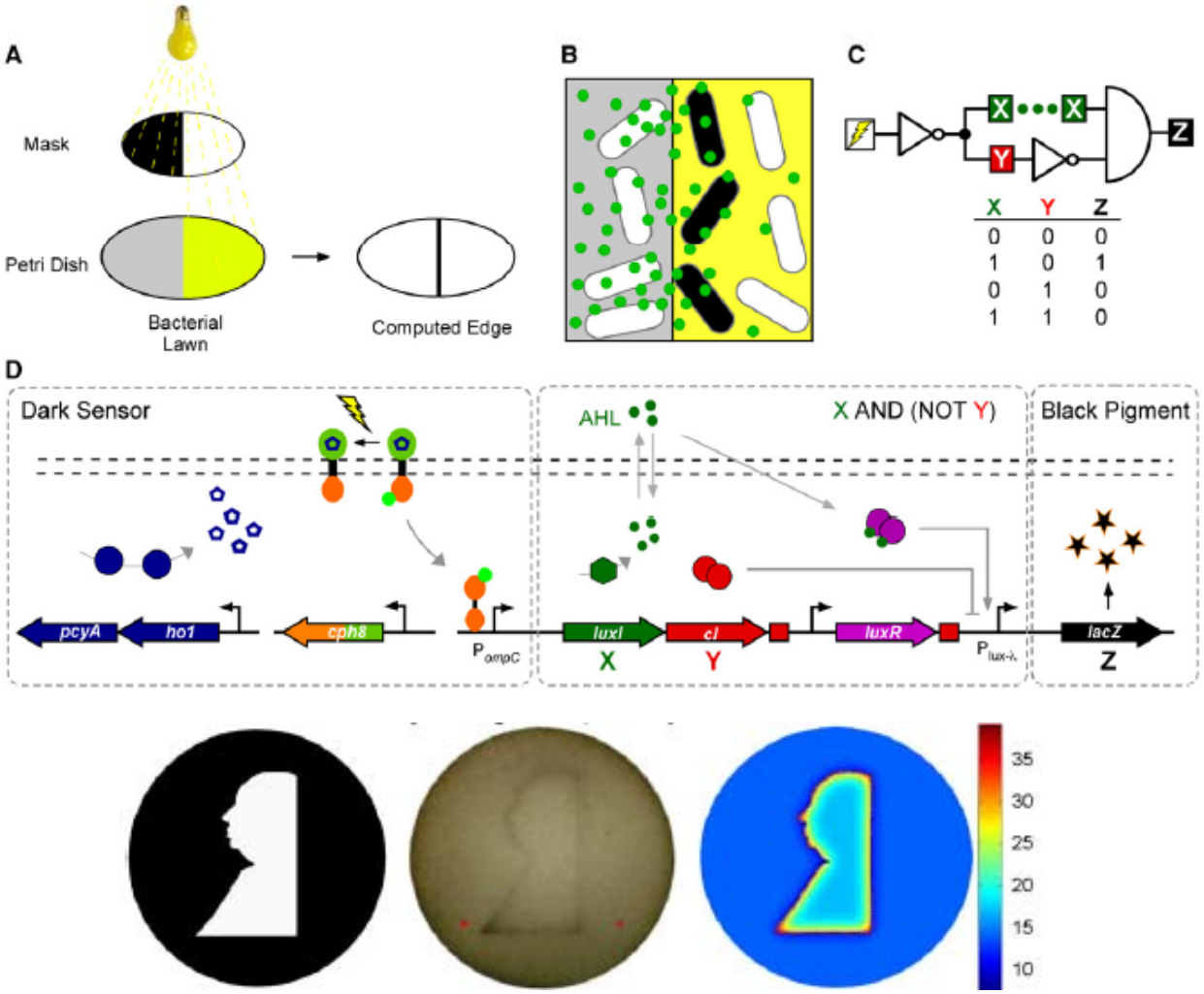
Postcards & snapshots so far

- genome re-engineering
- DNA based memory
- logic engineering
- circuit engineering
- system engineering

A Synthetic Genetic Edge Detection Program

Jeffrey J. Tabor,[1] Howard M. Salis,[1] Zachary Booth Simpson,[2,3] Aaron A. Chevalier,[2,3] Anselm Levskaya,[1] Edward M. Marcotte,[2,3,4] Christopher A. Voigt,[1,*] and Andrew D. Ellington[2,3,4]

1272 Cell *137*, 1272–1281, June 26, 2009 ©2009 Elsevier Inc.



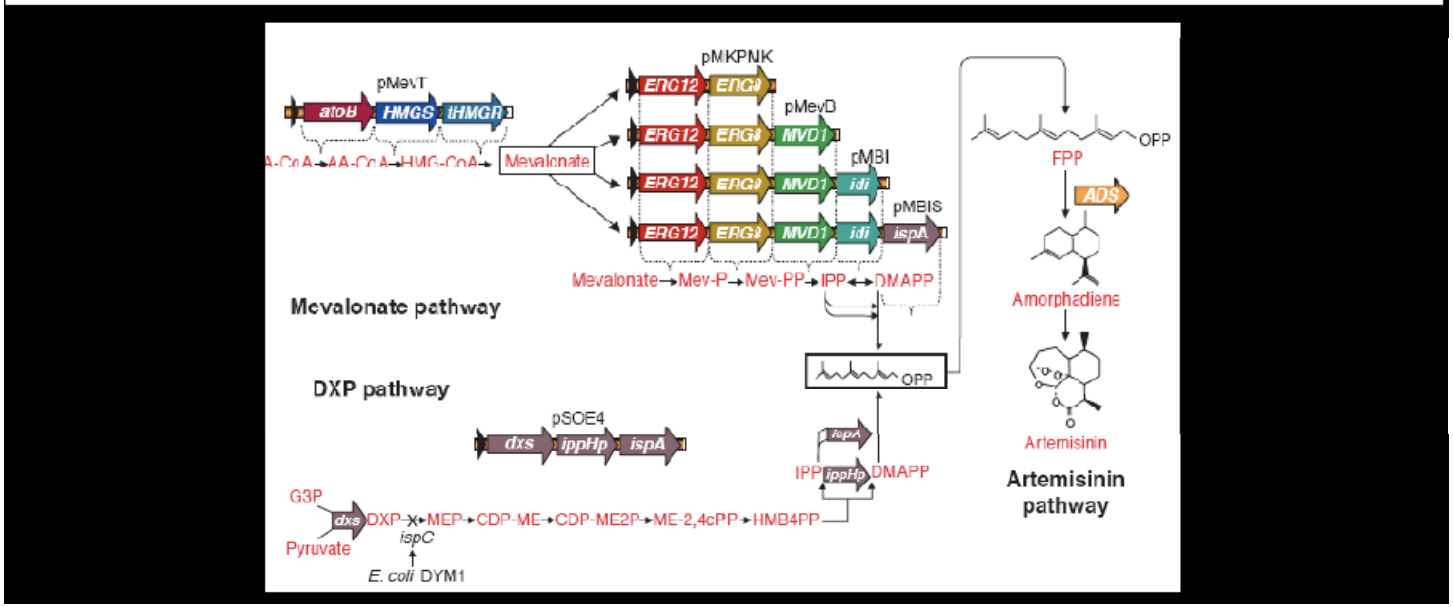
Postcards & snapshots so far

- DNA based memory
- circuit engineering
- logic engineering
- genome re-engineering

Engineering a mevalonate pathway in *Escherichia coli* for production of terpenoids

Vincent JJ Martin[1,2,3], Douglas J Pitera[1,3], Sydnor T Withers[1], Jack D Newman[1] & Jay D Keasling[1]

Isoprenoids are the most numerous and structurally diverse family of natural products. Terpenoids, a class of isoprenoids often isolated from plants, are used as commercial flavor and fragrance compounds and antimalarial or anticancer drugs. Because plant tissue extractions typically yield low terpenoid concentrations, we sought an alternative method to produce high-value terpenoid compounds, such as the antimalarial drug artemisinin, in a microbial host. We engineered the expression of a synthetic amorpha-4,11-diene synthase gene and the mevalonate isoprenoid pathway from *Saccharomyces cerevisiae* in *Escherichia coli*. Concentrations of amorphadiene, the sesquiterpene olefin precursor to artemisinin, reached 24 μg caryophyllene equivalent/ml. Because isopentenyl and dimethylallyl pyrophosphates are the universal precursors to all isoprenoids, the strains developed in this study can serve as platform hosts for the production of any terpenoid compound for which a terpene synthase gene is available.



Postcards & snapshots so far

- genome re-engineering
- DNA based memory
- logic engineering
- circuit engineering
- system engineering

doi:10.1016/j.jmb.2005.10.076 *J. Mol. Biol.* (2006) **355**, 619–627

JMB

Available online at www.sciencedirect.com

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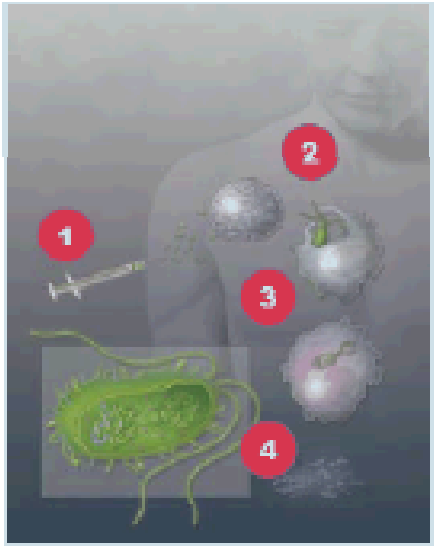
Environmentally Controlled Invasion of Cancer Cells by Engineered Bacteria

J. Christopher Anderson[1,3], Elizabeth J. Clarke[3], Adam P. Arkin[1,2*] and Christopher A. Voigt[2,3]



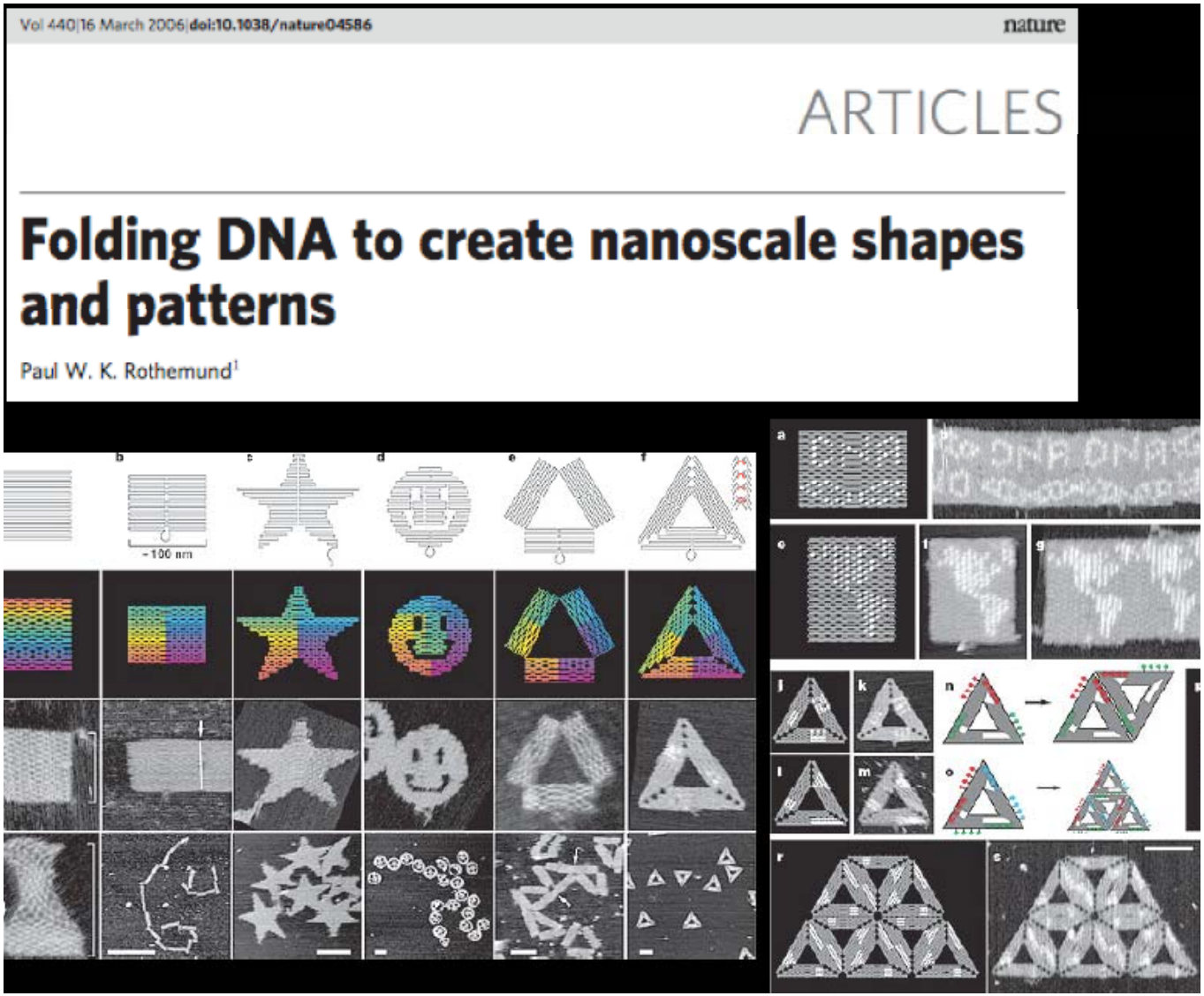
Tumor-killing bacteria

1. Engineered bacteria are injected into the bloodstream; polysaccharide molecules on their surfaces allow them to evade the immune system
2. When they detect the low-oxygen environment of a tumor, the bacteria produce invasion, a protein that allows them to infiltrate the cancer cells
3. The invasion binds to the cancer cells, prompting the cells to engulf the bacteria
4. The cancer cell bursts the bacterium, releasing an enzyme that is toxic to the cancer cell

Image courtesy Tami Tolpa

Postcards & snapshots so far

- genome re-engineering
- DNA based memory
- logic engineering
- circuit engineering
- system engineering
- biomaterials engineering



Vol 440|16 March 2006|doi:10.1038/nature04586

nature

ARTICLES

Folding DNA to create nanoscale shapes and patterns

Paul W. K. Rothemund[1]

Postcards & snapshots so far

- genome re-engineering
- DNA based memory
- logic engineering
- circuit engineering
- system engineering
- biomaterials engineering